

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:

Pears, D. A. *et al.*

Application No.: 10/568,146

Filed: September 25, 2006

Title: *Microencapsulated Catalyst-Ligand System,
Methods of Preparation and Methods of Use
Thereof*

Confirmation No.: 7751

Art Unit: 1793

Examiner: Qian, Y.

Attorney Docket No.: **HGX-012.01**

Mailstop: RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 23313-1450

DECLARATION UNDER 37 CFR § 1.132

Dear Sir:

I, Mohammed Nisar, declare as follows in connection with the above-captioned patent application:

1. I am an expert in the field of heterogeneous catalysis. I studied Applied Chemistry at De Montfort University, U.K., where I was awarded a BSc (Hons) in 1998. I then studied for a Masters degree at University of Manchester on "Synthesis and applications of polymer-supported catalysts" completing the course in 2001. I then joined Avecia Ltd in Manchester UK as a Research and Development chemist, and was part of the team that formed the spin-off catalyst technologies company Reaxa Ltd. A copy of my *curriculum vitae* is attached as **Exhibit A**.

2. I am currently employed as Research and Development Chemist at Reaxa Limited, Blackley, Manchester, England, the assignee of the entire interest in the above-captioned matter.

3. I am a named inventor on the above-identified matter.

4. I am aware of facts (e.g., experimental results and other data) pertinent to the claimed microencapsulated catalyst-ligand system.

5. Palladium acetate ($\text{Pd}(\text{OAc})_2$) was co-encapsulated with triphenylphosphine (PPh_3) ligands as follows. Due to the air-sensitive nature of ligands, the organic phase was prepared in a glove box under a nitrogen atmosphere. The organic phase was formed from $\text{Pd}(\text{OAc})_2$ (2.95 g, 98%) dissolved in chloroform (25.7 g) and then stirred for 10 minutes followed by addition of triphenylphosphine (1.72 g, 99%; 2:1 Pd/P molar ratio) and then stirred for a further 30 minutes. To this mixture, polymethylene polyphenylene di-isocyanate (PMPPI) (19.11 g) was added and the contents stirred for a further 60 minutes. This organic phase mixture was then added to an aqueous phase containing 40% REAX (sodium lignosulfonate) 100 M solution (3.95 g), 20% TERGITOL XD (polyoxypropylene polyoxyethylene ether of butyl alcohol) solution (1 g) and 25% Poly Vinyl Alcohol (PVOH) solution (1.98 g) in deionized water (83 mL) while shearing (using a FISHER 4-blade retreat-curve stirrer) at 500 rpm for 8 minutes. The reaction was maintained under inert atmosphere (N_2) throughout. After 8 minutes the shear rate was reduced to 250 rpm and few drops of de-foamer (DrewPLus S-4382) were added during the onset of polymerization (detected by carbon dioxide evolution). The suspension thus obtained was stirred at room temperature for a further 24 hours. The resulting microcapsules were then filtered through a polyethylene frit (20 micron porosity) and the capsules washed on a filter bed according to the following sequence: deionized water (5 x 100 mL), ethanol (3 x 100 mL), hexane (3 x 100 mL), and finally dried in a vacuum oven at 50°C.

6. In the microcapsules prepared as described in Paragraph 5 a sub-stoichiometric amount of phosphorous ligand to palladium is used (Pd/P molar ratio 2:1). Commonly used palladium phosphine complexes such as tetrakis(triphenyl)-phosphine palladium and bistris(triphenyl)phosphine palladium dichloride conversely contain phosphine in excess over palladium (Pd/P molar ratios 1:4 and 1:2 respectively). These complexes are therefore unlikely to form in the co-encapsulated catalyst-ligand systems. Moreover, due to stoichiometry, such commonly used complexes cannot predominate in the microcapsules prepared as in Paragraph 5.

7. In a commonly used palladium-phosphine complex, such as a tetrakis(triphenyl)-phosphine palladium complex, used in catalytic bond-forming reactions, the palladium is in an

oxidation state of zero (i.e., the palladium is present as palladium (0)).

8. X-ray photoelectron spectroscopy (XPS) has been used to study the oxidation state of palladium in the microcapsules prepared as described in Paragraph 5. The response from the electronic orbitals of metals in different oxidation states gives different peaks in this technique and thus provides information as to the oxidation state of the palladium in the microencapsulated beads. Data from such studies demonstrated that most of the palladium in phosphine-containing microencapsulated catalyst-ligand systems, when palladium is introduced as palladium (II) acetate (in which the palladium has an oxidation state of two), is present as palladium (II) and not present as palladium (0). In other words, the palladium in these beads does not appear to be present as a commonly used palladium-phosphine complex (in which the palladium is in an oxidation state of zero); instead, to the limits of detection it is present in the form of palladium (II) (e.g., as the palladium (II) acetate salt). Representative XPS data are attached as **Exhibit B**.

9. The attached XPS data demonstrates that most if not all of the palladium present in these microencapsulated catalyst-ligand systems is in an oxidation state other than zero (0).

10. All statements made herein of my own knowledge are true and all statements made on information and belief are believed to be true; and further that the undersigned acknowledges that any knowingly and willfully made materially false statements and the like are punishable by fine or imprisonment or both, under § 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,

Date: December 14, 2010


Mohammed Nisar, MSc.

Exhibit A

Mohammad Nisar

Profile

I am a highly successful technical support manager with over nine years experience of working in the fine chemical and pharmaceutical industry. Qualified as a chemist and gained experience in research and development before progressing career as technical expert with additional commercial role. Experienced in project management, strategic planning and commercial awareness of introducing new products into established industry.

Achievements

- Successfully developed and launched new products as 'greener alternatives' for use in the chemical and pharmaceutical industry.
- Holder of four patents as inventor for polymer-supported catalysts.
- Implementation of quality management system to gain ISO 9001 accreditation.
- Chemical Industries Association (CIA) and IChemE awards in 2004 for innovation and excellence.

Career Progression

Reaxa Ltd, Manchester 2005 – Present

- Technical support expert providing range of information and advice to major pharmaceutical organisations in adopting our proprietary new technology.
- Management of research and development projects from conception through to completion, including government funded projects with budgets up to £250K.
- Managing numerous key scientific contacts within the pharmaceutical and fine chemical industry.
- Technology transfer of chemical processes to external toll manufacturing partners based in UK and overseas.
- Technical presentations at customer sites and scientific conferences.
- Commercial support at pharmaceutical & chemical industry exhibitions.

Avecia Ltd, Manchester 2001-2005

- Working successfully as part of a team involved in research and development of polymeric products for commercial launch.
- Progressed to position of supervisor and chemist-in-charge with responsibilities managing placement students and laboratory safety adherence.
- Attending yearly scientific seminars to discuss research projects with colleagues from within company.

Redbridge Magistrates Court, Essex 1998-1999

- Working as legal aid officer responsible for processing legal aid applications and calculating contributions.
- Involved in assessment and recommendation, frequent contact with court officials, law professionals and outside agencies.

Hicksons & Welch Ltd, Yorkshire 1996-1997

- Twelve month industrial placement forming part of undergraduate degree as a research and development scientist.

Education and Qualifications

1999 - 2001 University of Manchester – MSc Polymer Science and Technology.

1994 - 1998 De Montfort University – BSc (Hons) Applied Chemistry.

Training

2008 - Course to assist in design and implementation of quality management system.

2006 - Commercial negotiating skills training course.

2005 - Commercial awareness training.

2004 - Process scale-up to multi-Kg

1996 - Fire safety and breathing apparatus training.

Professional Skills

- Proficient in the use of Microsoft Office software, internet and Outlook mail.
- Excellent written and verbal communication skills.

Exhibit B: XPS Analysis of Palladium containing microcapsules

Palladium encapsulated samples as follows were submitted for XPS analysis:

Sample Code (ASG1035-)	Material Name	Material Description
3022	Pd EnCat 40	Pd acetate in polyurea polymer
3023	Pd EnCat TPP30	Pd acetate and co-encapsulated triphenylphosphine in polyurea polymer
3024	Pd EnCat TPP40	Pd acetate and co-encapsulated triphenylphosphine in polyurea polymer
3025	Pd EnCat TOTP30	Pd acetate and co-encapsulated tri-ortho-tolylphosphine in polyurea polymer
3026	Pd EnCat TOTP40	Pd acetate and co-encapsulated tri-ortho-tolylphosphine in polyurea polymer
3027	Pd(0) EnCat 40	Pd(0) nanoparticles in polyurea polymer

The 30 and 40 after the EnCat describes the porosity of the polymer matrix. The two types of samples are otherwise prepared identically.

The XPS analysis demonstrates that all the co-encapsulated phosphine EnCat samples (sample codes 3023-3026) contain Pd in the same oxidation state and that this oxidation state is the same as the EnCat containing only Pd acetate (sample code 3022). This is shown by a strong peak at 338.5 - 339 eV due to Pd 3d ("Position" column, first row of each sample results set).

This is a different oxidation state to a sample where palladium is known to be in the zero oxidation state (sample code 3027). This is shown by a peak from this sample at 337 eV.

The analysis report follows.

Samples Analysed by XPS

Each powder / bead sample was sprinkled over the surface of double sided tape (approx 10mm x 10mm) to give as complete a coverage as possible. It is possible that some silicon signal is attributable to exposed tape areas.

Charge correction used a CAE=20eV C1s scan assuming the peak of the hydrocarbon peak was at 285eV.

Sample designations:-

- ASG10353022
- ASG10353023
- ASG10353024
- ASG10353025
- ASG10353026
- ASG10353027

XPS Quantification Results

XPS Quantification - Atomic Concentrations

(Click on it to open Excel data)

Quantification results taken from CAE=50eV survey scans (0.5eV Step) and the Pd3d narrow scan

Sample code	Name	Position	FWHM	R.S.F.	Area	% Conc.
3022 Pd Encut 40	Pd 3d	338.9	2.404	16.04	41523.9	1.194
	S 2p	169.5	1.978	1.677	2848.4	0.763
	Si 2p	103	2.328	0.8401	8063.6	4.427
	C 1s	286	2.801	1	143298.9	66.087
	O 1s	533.5	2.801	2.93	155132.5	24.418
	N 1s	401.5	2.049	1.8	12084.2	3.091
3023	Pd 3d	338	2.405	16.04	19284	0.519
	S 2p	168.5	2.334	1.677	2861.5	0.738
	Si 2p	103	2.472	0.8401	8667.6	4.826
	C 1s	286	2.535	1	169218.1	73.191
	O 1s	533.5	2.917	2.93	110039.6	16.244
	N 1s	401.5	2.183	1.8	18234	4.381
3024	Pd 3d	338.4	2.653	16.04	36538.8	0.915
	S 2p	169	2.134	1.677	2908.9	0.598
	Si 2p	103	2.108	0.8401	3711.9	1.77
	C 1s	285.5	2.547	1	188788.9	75.648
	O 1s	533	3.286	2.93	112021.7	16.319
	N 1s	401	2.232	1.8	23756.5	5.288
	P 2p	133	1.759	1.192	1372	0.461
3025	Pd 3d	338.4	2.279	16.04	23626.8	0.606
	S 2p	168.5	2.458	1.677	3537.9	0.867
	Si 2p	103.5	2.482	0.8401	4941.8	2.419
	C 1s	285.5	2.657	1	178815.4	73.57
	O 1s	533.5	3.103	2.93	124898.7	17.527
	N 1s	400.5	2.658	1.8	20940.9	4.761
	P 2p	132.5	1.373	1.192	725.4	0.25
3026	Pd 3d	338.5	2.46	16.04	27183.1	0.716
	S 2p	169	1.712	1.677	3654	0.885
	Si 2p	103.5	2.363	0.8401	6883.2	3.512
	C 1s	286	2.675	1	173888.5	73.504
	O 1s	533.5	3.256	2.93	110480.3	15.93
	N 1s	401	2.463	1.8	20301	4.765
	P 2p	133	2.365	1.192	1914.4	0.678
3027 Pd (o)	Pd 3d	337.2	0.513	16.04	3374.4	0.085
	Si 2p	102.5	4.197	0.8401	3520	1.882
	C 1s	286	2.819	1	173386.3	77.853
	O 1s	533.5	3.845	2.93	79784.5	12.23
	N 1s	401	2.587	1.8	31652.2	7.9